NEUROFIT SAS

Pre-Clinical CRO

CNS & PNS preclinical Services

Semaglutide's cognitive rescue: insights from rat and mouse models of Alzheimer's disease

E. ANDRIAMBELOSON, C. DUCHEMIN, B. HUYARD, F. LAUGA, L. PETER, E. POIRAUD, S. WAGNER;

Introduction / Objective

• Semaglutide is a drug from the Glucagon-like peptide-1 (GLP-1) class that promotes weight loss and improves hyperglycemia.

• GLP-1 drugs appear to affect multiple aspects of the metabolic system implicated in Alzheimer's disease, including amyloid and inflammation pathways.

• The present study investigates the impact of Semaglutide treatment on:

- **in-vivo amyloid-β (Aβ) -induced memory deficit in the rats**
- **in-vivo inflammation (LPS) -induced cognitive deficit in mice**
- **in-vitro brain inflammation (LPS) -induced neuronal death in glia-neuron coculture system**

In-vivo experimental protocol

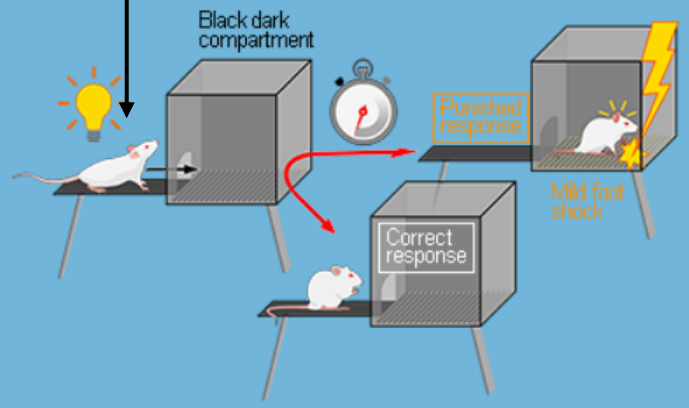
Placebo

«i.c.v $A\beta_{25-35}$ -injected rats»

Semaglutide

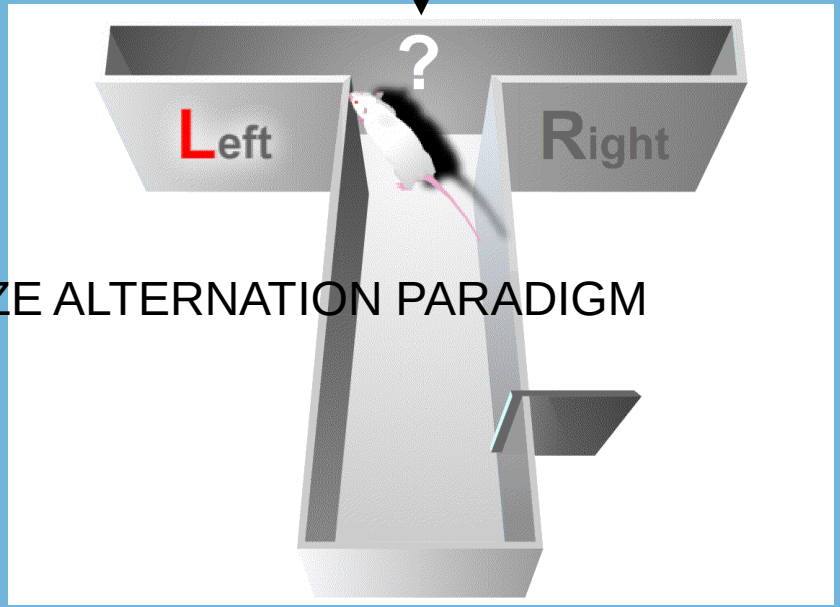
«LPS-injected mice»

PASSIVE AVOIDANCE PARADIGM



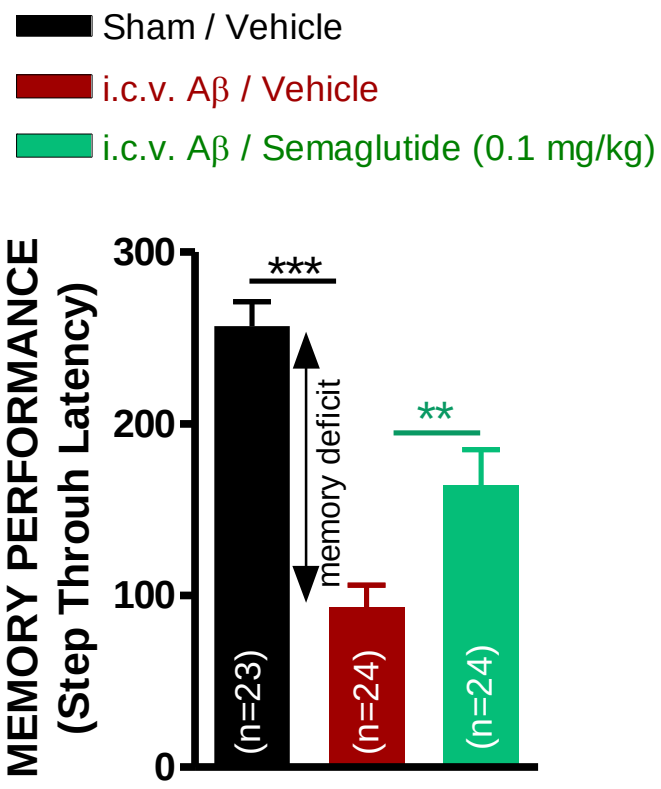
Memory performance is positively correlated with the latency to leave the bridge and avoid the adverse stimulus, thus the better the recollection, the greater the "**step through latency**".

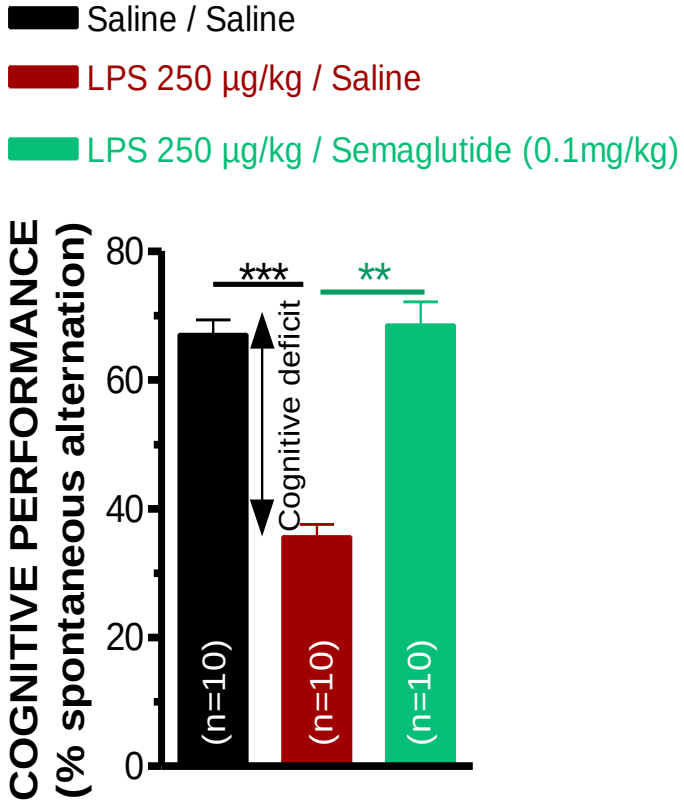
T-MAZE ALTERNATION PARADIGM



The lower the percentage of alternation between the left and right arms of the T-maze, the poorer the cognitive performance of the mice

Impact of Semaglutide treatment on rodents with memory and cognitive deficit

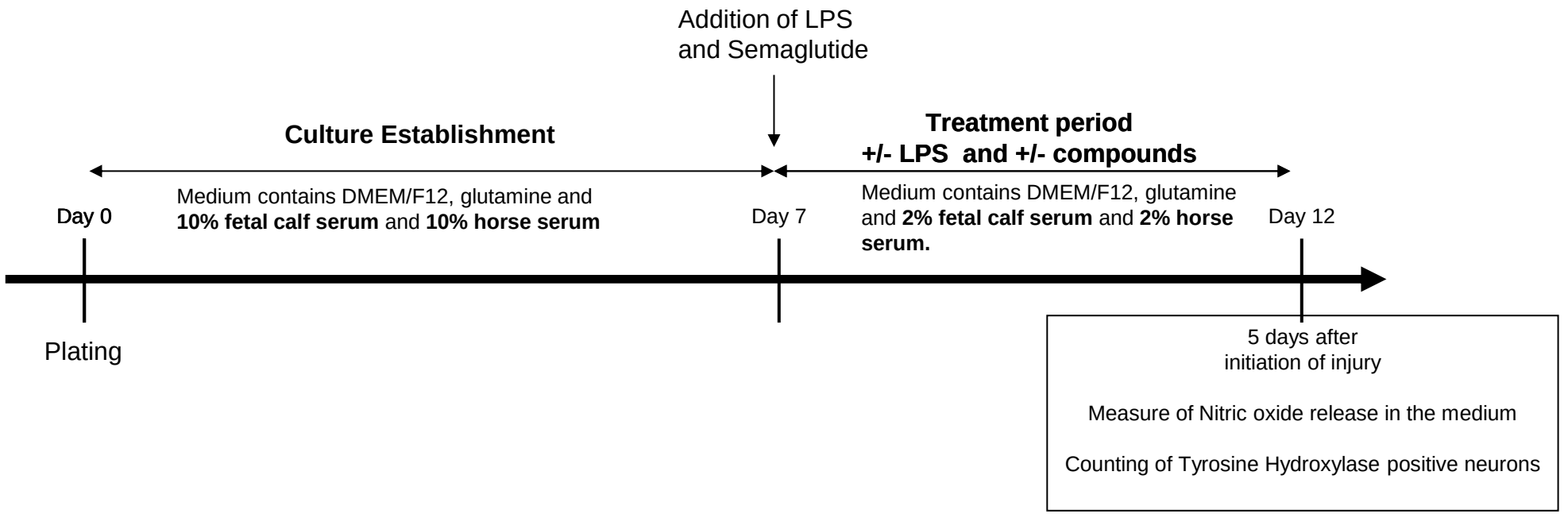




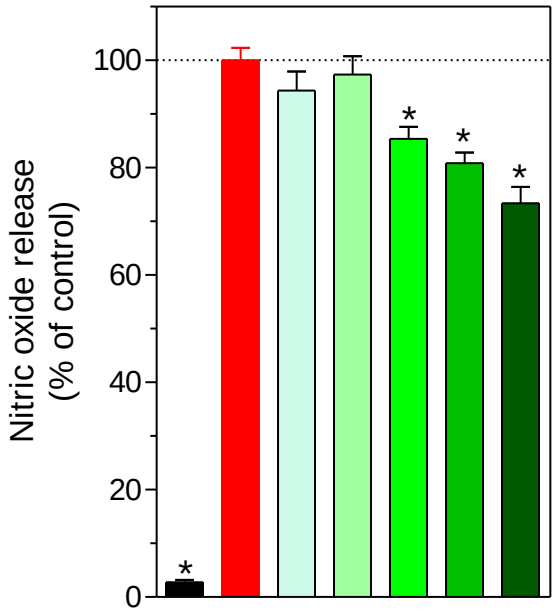
⇒ One week Semaglutide significantly improves the memory deficit in rats i.c.v. Aβ injections.

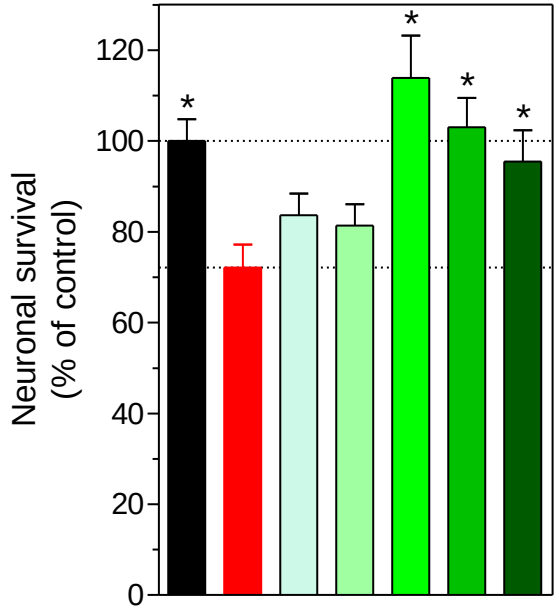
⇒ One week Semaglutide fully restores the cognitive deficit of LPS-treated mice, suggesting a potential anti-inflammatory effect.

Primary neuronal culture experimental protocol



Impact of Semaglutide treatment on Neuronal death and nitric oxide release induced by LPS in glia-neuron coculture





⇒ Dose-response inhibition of nitric oxide release by Semaglutide in glia-neuron co-cultures, which suggests a potential anti-inflammatory action Semaglutide.

⇒ Dose-response inhibition of LPS-induced neuronal death by Semaglutide in glia-neuron co-cultures, most probably via its anti-inflammatory action.

Conclusion

- These results support the beneficial effect of Semaglutide treatment against amyloid-β -induced cognitive deficit.
- They also indicate that an anti-inflammatory effect of Semaglutide could be one of the primary mechanisms behind this benefit.